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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/334,325	06/16/1999	STEWART A. CEDERHOLM-WILLIAMS	CV0276A	5209

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EXAMINER

CHEN, SHIN LIN

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 06/05/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/334,325	CEDERHOLM-WILLIAMS, STEWART A.	
	Examiner Shin-Lin Chen	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 18 April 2002.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1,2 and 13-16 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1,2 and 13-16 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____	6) <input type="checkbox"/> Other: _____

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DETAILED ACTION

Applicant's amendment filed 4-18-02 has been entered. Claims 1, 2 and 13-16 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 2 and 13-16 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of transforming a cell *in vitro* by applying a nucleic acid and a pliable, adhesive fibrin gel to said cell, does not reasonably provide enablement for a method of transforming a cell *in vivo* by applying a nucleic acid and a pliable, adhesive fibrin gel to said cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims and is repeated for the reasons set forth in the preceding Official action mailed 12-19-01 (Paper No. 15). Applicant's arguments filed 4-18-02 have been fully considered but they are not persuasive.

Applicant argues that it was well known in the art that *in vivo* transfection can give rise to immune response and there are more than sufficient vectors in the art which are not disabled in their effect by an immune response. Applicant further argues that vector-based vaccines were

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known and desirable and are enabled (amendment, p. 2, 3). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 12-19-01 (Paper No. 15) and that the specification fails to provide adequate guidance and evidence to enable the use of nucleic acid and pliable, adhesive fibrin gel as a vaccine in the claimed method to stimulate immune response *in vivo*. No evidence of record indicates that the nucleic acid itself can stimulate sufficient immune response in a subject *in vivo* so as to provide therapeutic effect for a particular disease or disorder. In case that the protein product encoded by the nucleic acid is desirable to stimulate immune response *in vivo*, there is no evidence of record that indicates sufficient protein product is expressed *in vivo* to stimulate sufficient immune response *in vivo* for treating a particular disease or disorder. Thus, the specification fails to provide enabling disclosure for the use of nucleic acid and pliable, adhesive fibrin gel as a vaccine in the claimed method to stimulate immune response *in vivo*.

In fact, the intended use of the nucleic acid and pliable, adhesive fibrin gel is for gene delivery in *in vivo* gene therapy in light of the specification (see specification, p. 2-4). As discussed in the preceding Official action mailed 12-19-01 (Paper No. 15), host immune response poses problems to the use of various vector and virus in gene transfer *in vivo*. Further, no teachings are present within the specification in regard to how to transform cells with any nucleic acid in any vector or any virus containing said nucleic acid by using fibrinogen composition or fibrin gel, how the nucleic acid entrapped in fibrin gel can be taken up by cells, and whether the nucleic acid taken up by cells can be expressed in said cells *in vivo*. Thus, the

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specification fails to provide enabling disclosure for the use of nucleic acid and pliable, adhesive fibrin gel for gene delivery *in vivo*. One skilled in the art at the time of the invention would require undue experimentation to practice over the full scope of the invention claimed.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:
 - (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.
4. Claims 1, 2 and 13-16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Donovan, 1998 (US patent No. 5,833,651) and is repeated for the reasons set forth in the preceding Official action mailed 12-19-01 (Paper No. 15). Applicant's arguments filed 4-18-02 have been fully considered but they are not persuasive.

Applicant argues that Office action at page 6 suggest that Donovan teaches using fibrin other than using a tent is in error. Applicant further argues that the meaning of "fibrin monomer" in Donovan is different from that as defined in the specification (amendment, p. 3). This is not found persuasive because of reasons of record. Donovan teaches the stent can be loaded with virus by mixing a solution of fibrin monomer and virus containing nucleic acid to form a polymer, i.e. fibrin gel, which can be used to deliver the virus to the cell at column 13. The Office does not imply that the mixture can be delivered to cell via apparatus other than stent.

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Donovan teaches using a **solution** of "fibrin monomer" which would indicates that the "fibrin monomer" is **non-polymerized** so that it is in a **solution**. Therefore, the term "fibrin monomer" in Donovan has the same meaning as that defined in the specification of the present application, i.e. stabilized in essentially non-polymerized form. It would be obvious and well known in the art for how to stabilize "fibrin monomer" in a non-polymerized form.

Applicant argues that there is no teaching in Donovan to entrap nucleic acid adhered to a cell in a pliable fibrin gel and cites Winner International Royalty Corp vs Wang (amendment, p. 3, 4). This is not found persuasive because of reasons of record. It would have been obvious for one of ordinary skill at the time of the invention to apply a nucleic acid to cells first then adhering a pliable, adhesive fibrin to said cells to entrap said nucleic acid because adding a nucleic acid to cells before, during, or after the formation of a pliable, adhesive fibrin gel are for the same purpose of entrapping the nucleic acid in fibrin gel to deliver said nucleic acid to said cells and would be obvious for one of ordinary skill.

Conclusion

No claim is allowed.

5: **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Scott Priebe can be reached on (703) 308-7310. The fax phone number for this group is (703) 308-4242.

Questions of formal matters can be directed to the patent analyst, Patsy Zimmerman, whose telephone number is (703) 305-2758.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

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Shin-Lin Chen, Ph.D.

Scott D. Priebe

SCOTT D. PRIEBE, PH.D.
PRIMARY EXAMINER